one or more nucleic acid molecules encoding one or more antigens which comprise said T cell epitope. Support for this amendment can be found throughout the specification, for example, at page 11, lines 8-15. No new matter has been added.

Claim 7 has been amended to recite the method of Claim 1 wherein the level of human T cell response to the processed antigen is indicated by the level of release of one or more cytokines or level of lysis of the human antigen presenting cells. Support for this amendment can be found throughout the specification, for example, at page 13, lines 7-8, and page 14, lines 3-5. No new matter has been added.

Claim 8 has been amended to correct minor typographical errors. Support for this amendment can be found throughout the Specification and in the originally filed claim. No new matter has been added.

Claim 11 has been amended to recite that the two or more distinct vaccine compositions in the group each having one or more nucleic acid molecules encoding one or more antigens which comprise a specific T cell epitope. Support for this amendment can be found throughout the specification, for example, at page 11, lines 8-15. No new matter has been added.

Claim 23 has been added to recite a method for optimizing the T cell response against a T cell epitope. Support for this claim can be found throughout the specification, for example, at page 8, lines 13-23. No new matter has been added.

Rejection of Claims 1, 4-8, 11, 17, and 20-22 Under 35 U.S.C. §112, second paragraph

Claims 1, 4-8, 11, 17, and 20-22 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

Specifically the Examiner states that Claims 1 and 11 are unclear in the preamble because it is not clear as to whether "a defined T-cell epitope" is a single epitope, common to all members of the group of vaccines, or whether this is a unique epitope for each of the members of the group.

Claims 1 and 11 have been amended to clarify that which Applicant regards as the invention. The preamble clearly recites that the vaccine compositions within the group of vaccine compositions are distinct from each other and that each have one or more nucleic acid

molecules encoding one or more antigens which comprise a specific T cell epitope. Thus, while the compositions assayed are distinct, they are characterized by a common epitope. Reconsideration and withdrawal of the rejection as it applies to these claims are respectfully requested.

Additionally, the Examiner states that in Claim 1, part (b) "defined peptide" lacks antecedent basis. Claim 1 has been amended to remove the word "defined", thus rendering the rejection moot. Reconsideration and withdrawal of the rejection as it applies to this claim are respectfully requested.

Moreover, the Examiner states that Claim 7 is unclear in relation to base Claim 1. Applicants have amended Claim 7 as suggested by the Examiner. Reconsideration and withdrawal of the rejection as it applies to this claim are respectfully requested.

Rejection of Claims 1, 4-8, 11, 17, and 20-22 Under 35 U.S.C. §112, first paragraph

Claims 1, 4-8, 11, 17, and 20-22 are rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

To support this rejection the Examiner states that there was no original disclosure that the candidate vaccines in the group of vaccine compositions have "a defined T cell epitope", irrespective of whether such "defined" epitope is common to all members or is a unique epitope for each of the members of the group. Thus, according to the Examiner, the phrase "a defined T cell epitope" constitutes new matter.

Applicants have amended the claims to recite "a vaccine composition in a group consisting of two or more distinct vaccine compositions each having one or more nucleic acid molecules encoding one or more antigens which comprise a specific T cell epitope ...". Support for this amendment can be found throughout the Specification. For example, at page 4, lines 13-14, Applicants state that "the T cells are T cell clones which are ***specific*** for a T cell epitope in at least one of the antigens." Additionally, Applicants state at page 10, lines 4-5, "preferably, the T cells are ***specific*** for a particular epitope within the antigen." Moreover, at page 11, lines 8-15, Applicants teach that "the T cell are clones which are ***specific*** for a particular epitope, and the

vaccine composition includes at least one antigen which comprises the epitope or at least one nucleic acid molecule encodine at least one antigen which comprises the epitope. In this embodiment, response of the ***epitope-specific T cell clones*** to antigen-presenting cells which have been contacted with the experimental vaccine composition indicates that the vaccine composition is able to effect the presentation of the epitope on the surface of the antigen-presenting cells in combination with an MHC I or MHC II molecule." (emphasis added)

Therefore, no new matter has been added to the claims, as amended. Reconsideration and withdrawal of the rejection is respectfully requested.

Rejection of Claims 1, 5-8, 11, 17 and 20 Under 35 U.S.C. §103(a)

Claims 1, 5-8, 11, 17 and 20 are rejected under 35 USC 103(a) as being unpatentable over Tal *et al.* (U.S. 5,763,284)("Tal") in light of Sette *et al.* (Nature 328, 397 (1987))("Sette").

The Examiner states that Tal shows an assay essentially corresponding to the instantly claimed assays (col. 10, line 34 through col. 12, line 21). Tal describes an assay to identify peptides useful in eliciting a desired immune response conducted by the following steps:

(a) Antigen presenting cells are contacted with a fusion polypeptide of the invention;

(b) T cells carrying the T cell receptor specific to the fusion polypeptide are obtained such as from a T cell hybridoma of interest;

(c) T cells carrying the T cell receptor specific to the fusion polypeptide are contacted with the antigen presenting cells of step 1;

(d) After a suitable period of time, modulation of the activity of the T cells by the fusion polypeptide is measured.

Tal goes on to state that "these *in vitro* assays can be employed to select and identify peptide(s) that are capable of modulating the activity of T cell receptor." (See Tal col. 11, lines 53-64) Specifically, DNA sequences encoding either a library of random peptides or selected peptides can be cloned into expression vectors and used in the assay as described above.

The Examiner relies upon Sette as a secondary reference. The Examiner states that the exemplified polypeptide in examples 9 and 10 of Sette has a defined T-cell epitope. Therefore, according to the Examiner, candidate vaccines with defined T-cell epitopes would have been obvious.

Applicant's claimed invention, as amended, is directed to a method for assessing the ability of a vaccine composition in a group consisting of two or more distinct vaccine compositions each having one or more nucleic acid molecules encoding one or more antigens which comprise a specific T cell epitope, to stimulate a monoclonal human T cell response, said method comprising the steps of:

(1) contacting human antigen presenting cells in culture with the vaccine composition, thereby, if one or more of the nucleic acid molecules are taken up and processed by said antigen presenting cells, producing one or more processed antigens;

(2) contacting said antigen presenting cells of step (1) with monoclonal human T cells having a T cell receptor specific for the peptide encoded by said nucleic acid molecule(s) encoding one or more antigens which comprise said T cell epitope and known HLA allele for said T cells under conditions sufficient for said T cells to respond to the processed antigen;

(3) determining the level of said T cells' response to the processed antigen; and, if the vaccine composition exceeds a predetermined level of said T cells' response,

(4) assessing the vaccine composition in one or more human subjects.

Applicants method is used to determine the efficacy of one or more distinct vaccine compositions in a group of vaccine compositions. For example, as taught by Applicants at page 15, lines 29-31, the distinct vaccine compositions include the same antigen(s), but different vectors, adjuvants, concentrations, vehicles or excipients can be compared to determine the conditions necessary for optimal efficacy.

The efficacy of a vaccine for use in humans depends upon the ability of the vaccine formulation to elicit an immune response which is sufficient to provide protection against subsequent challenge with the pathogen. Tal only teaches an assay that can be used to determine if a polypeptide can be processed by antigen presenting cells to elicit a T cell response. However, Tal neither teaches how to prepare a vaccine composition based on the nucleic acid and/or polypeptide for use in humans, nor how to test the efficacy of a vaccine composition *in vitro*. In contrast, Applicants teach a method that uses an antigen, that elicits a predetermined level of T cell response, in an *in vitro* test to determine the human response to an experimental

vaccine construct comprising said antigen, which would allow the rapid evaluation of large numbers of candidate vaccine compositions within a short period of time and at a reasonable cost, thereby increasing the possibility that effective vaccine compositions will be discovered.

Therefore, Applicants claimed invention, as amended, is non-obvious over the prior art. Reconsideration and withdrawal of the rejection are respectfully requested.

CONCLUSION

In view of the above amendments and remarks, it is believed that all claims are in condition for allowance, and it is respectfully requested that the application be passed to issue. If the Examiner feels that a telephone conference would expedite prosecution of this case, the Examiner is invited to call the undersigned at (978) 341-0036.

Respectfully submitted,
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Dated: 11/25/02

MARKED UP VERSION OF AMENDMENTS

Specification Amendments Under 37 C.F.R. § 1.121(b)(1)(iii)

Replace the paragraph at page 4, lines 12 through 18 with the below paragraph marked up by way of bracketing and underlining to show the changes relative to the previous version of the paragraph.

Preferably, the vaccine composition includes at least one antigen which comprises a T cell epitope, and the T cells are T cell clones which are specific for a T cell epitope in at least one of the antigens. In one embodiment, the T cells are CD8+ T cells and the vaccine composition includes at least one antigen comprising [antigen] a CD8 epitope. In this embodiment, the T cell response to the processed antigen can be, for example, T cell proliferation, cytolysis of the antigen presenting cells or the production of one or more cytokines.

Claim Amendments Under 37 C.F.R. § 1.121(c)(1)(ii)

1. (Thrice Amended) A method for assessing the ability of a vaccine composition in a group consisting of two or more distinct vaccine compositions each having [a defined human T cell epitope or] one or more nucleic acid molecules encoding one or more antigens which comprise [said] the same T cell epitope, to stimulate a monoclonal human T cell response, said method comprising the steps of:

   (a) contacting human antigen presenting cells in culture with the vaccine composition, thereby, if [said T cell epitope or] one or more of the nucleic acid molecules are taken up and processed by said antigen presenting cells, producing one or more processed antigens;

   (b) contacting said antigen presenting cells of step (a) with monoclonal human T cells having a T cell receptor specific for the [defined human T cell epitope or] defined peptide encoded by said nucleic acid molecule(s) encoding one or more antigens which comprise said T cell epitope and known HLA allele for said T cells under conditions sufficient for said T cells to respond to the processed antigen;

   (c) determining the level of said T cells' response to the processed antigen; and, if the vaccine composition exceeds a predetermined level of said T cells' response,

(d) assessing the vaccine composition in one or more human subjects.

7. (Twice Amended) The method of Claim 1 wherein the level of human T cell response to the processed antigen is indicated by the level of release of one or more cytokines or level of lysis of the human antigen presenting cells.

8. (Twice Amended) The method of Claim 1 wherein the level of human T cell response to the processed antigen [which] is measured [is] by the level of release of one or more cytokines or the level of stimulated formation of antibodies by B cells.

11. (Thrice Amended) A method for selecting one or more vaccine compositions from among a group consisting of two or more distinct vaccine compositions for assessment in a human, said vaccine compositions each comprising [a defined human T cell epitope or] one or more nucleic acid molecules encoding one or more antigens which comprise [said] the same T cell epitope, said method comprising the steps of:

(a) contacting human antigen presenting cells in culture with a vaccine composition selected from among said group of vaccine compositions, thereby, if [said T cell epitope or] one or more of the nucleic acid molecules encoding one or more antigens which comprise said T cell epitope are taken up and processed by said antigen presenting cells, producing one or more processed antigens;

(b) contacting said antigen presenting cells of step (a) with monoclonal human T cells under conditions sufficient for said T cells to respond to one or more of the processed antigens;

(c) determining the level of said T cells' response to one or more of the processed antigens;

(d) repeating steps (a), (b) and (c) with each additional vaccine composition in the group; and

(e) selecting at least one vaccine composition that exceeds a predetermined level of said T cells' response for assessment in one or more human subjects.